Control of Embryonic Stem Cell Lineage Commitment by Core Promoter Factor, TAF3.

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Public Summary:
Deciphering the molecular basis of pluripotency is fundamental to our understanding of development and embryonic stem cell function. Here, we report that TAF3, a gene regulatory factor, is highly enriched in ES cells. In this context, TAF3 is required for endoderm lineage differentiation and prevents premature specification of neuroectoderm and mesoderm. Interactions between TAF3 and regulatory proteins CTCF and cohesin were observed, suggesting that these proteins work together to maintain pluripotency. Together, our findings support a new role of TAF3 in mediating long-range gene regulatory interactions that safeguard the finely-balanced transcriptional programs underlying pluripotency.

Scientific Abstract:
Deciphering the molecular basis of pluripotency is fundamental to our understanding of development and embryonic stem cell function. Here, we report that TAF3, a TBP-associated core promoter factor, is highly enriched in ES cells. In this context, TAF3 is required for endoderm lineage differentiation and prevents premature specification of neuroectoderm and mesoderm. In addition to its role in the core promoter recognition complex TFIID, genome-wide binding studies reveal that TAF3 localizes to a subset of chromosomal regions bound by CTCF/cohesin that are selectively associated with genes upregulated by TAF3. Notably, CTCF directly recruits TAF3 to promoter distal sites and TAF3-dependent DNA looping is observed between the promoter distal sites and core promoters occupied by TAF3/CTCF/cohesin. Together, our findings support a new role of TAF3 in mediating long-range chromatin regulatory interactions that safeguard the finely-balanced transcriptional programs underlying pluripotency.